University of Minnesota
The University Library
Minneapolis 14 Minn.

VOLUME XI February 1955 NUMBER 2

UNIVERSITY OF MINNESOTA LIBRARY
RECEIVED
AUG 11 1955

Clinical Proceedings

OF THE

CHILDREN'S HOSPITAL

WASHINGTON, D. C.

ADENOMATOUS POLYPS OF THE RECTUM AND COLON IN CHILDREN. *Alejandro F. Castro, M.D.* 29

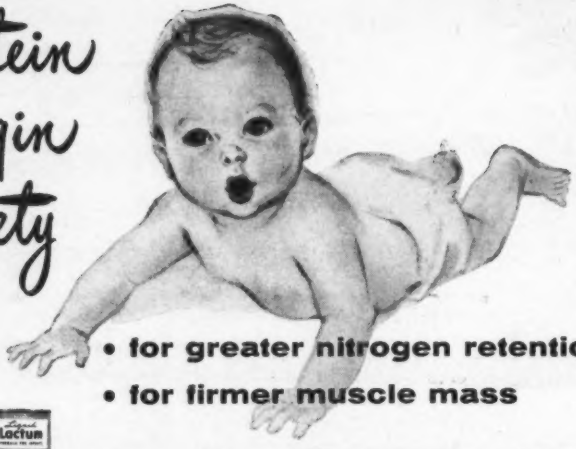
PROPHYLAXIS IN RHEUMATIC FEVER. SPECIAL REPORT. *Joseph M. LoPresti, M.D., John O. Nestor, M.D.* 32

ACUTE NEPHRITIS COMPLICATING AN ILLNESS RESEMBLING INFECTIOUS MONONUCLEOSIS. A CASE REPORT. *George J. Cohen, M.D.* 38

CLINOCO-PATHOLOGICAL CONFERENCE. DISCUSSANT: *Dr. George W. Ware* 42

SUGGESTED METHOD OF SCORING FOR A TISSUE COMMITTEE. EDITORIAL. *Ralph D. Whitley, M.D.* 46

Provides a protein margin of safety



- **for greater nitrogen retention**
- **for firmer muscle mass**

LIQUID

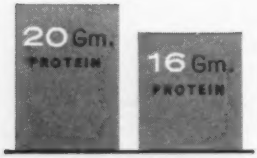
POWDERED

LACTUM

NUTRITIONALLY SOUND FORMULA FOR INFANTS

In the bottle-fed infant, a higher protein intake, with greater nitrogen retention, results in firmer muscle mass, better tissue turgor and better motor development.[1] A protein intake that does not maintain positive nitrogen balance "cannot be considered optimal or even safe for any length of time."[2]

During the first year of life, the infant's nourishment is derived primarily from his formula. Hence it is especially important that the formula be generous in protein. The usual Lactum® feedings provide 2 Gm. protein per pound of body weight—25% more than the Recommended Daily Allowance of 1.6 Gm. per pound (3.5 Gm. per kilogram).



Lactum formula for a 10 lb. infant

Recommended Daily Allowance for a 10 lb. infant

1. Jeans, P. C., in A.M.A. Handbook of Nutrition, Philadelphia, Blakiston, 1951, pp. 275-298. 2. Stare, F. J., and Davidson, C. S., in The Proteins, American Medical Association, 1945.

MEAD JOHNSON & COMPANY • EVANSVILLE, INDIANA, U.S.A. MEAD

MEAD, JOHNSON & COMPANY, Suite 419 Eig Building, 8641 Colesville Road, Silver Spring, Maryland. JUniper 9-1222

CLINICAL PROCEEDINGS
OF THE CHILDREN'S HOSPITAL
13th and W Streets, Washington 9, D. C.

EDITORS FOR FEBRUARY

GRACE H. GUIN, M.D. RALPH D. WHITLEY, M.D.

EDITOR

ROBERT H. PARROTT, M.D.

MANAGING EDITORS

FREDERIC G. BURKE, M.D.
JOSEPH M. LOPRESTI, M.D.
E. CLARENCE RICE, M.D.
SYDNEY ROSS, M.D.

ASSOCIATE EDITORS

JOHN BAYLY, M.D.
ROGER BERGSTROM, M.D.
STANLEY L. BLUMENTHAL, M.D.
ALLEN B. COLEMAN, M.D.
GORDON W. DAISLEY, M.D.
GRACE H. GUIN, M.D.
HANS G. KEITEL, M.D.
FRANCIS MASTROTA, M.D.
JOHN O. NESTOR, M.D.
MARSHALL M. PARKS, M.D.
DAVID A. ST. MARTIN, M.D.
JAMES H. STALLINGS, JR., M.D.
GEORGE WILLIAM WARE, M.D.
CHARLES R. WEBB, M.D.
RALPH D. WHITLEY, M.D.

GENERAL MANAGER

THELMA WALLER

CONTRIBUTING EDITORS FROM THE RESIDENT STAFF: CONRADO BOGAERT, M.D.; ROBERT L. BREGMAN, M.D.; GEORGE J. COHEN, M.D.; ALLEN B. MARANS, M.D.; JAMES W. OBERMAN, M.D.; ROLAND W. PENICK, M.D.; YOWALAKSN ARTHACHINTA, M.D.; JOSEPH M. ARIA, M.D.; VENETIA BARBA, M.D.; J. MARIO CHAVEZ, M.D.; JAMES A. DAVIS, JR., M.D.; ALVIN GOLDMAN, M.D.; PHYLLIS J. HAGEMAN, M.D.; FRANCES D. HANUSIK, M.D.; WALTER J. PACOSA, M.D.; NATIVIDAD PANGAN, M.D.; DORIS PLOUGH, M.D.; LUCAS RUBIO, M.D.; BENO S. VAJDA, M.D.; PIO G. VERA CRUZ, M.D.; ENID M. GILBERT, M.D.; AND RUDOLPH J. HURSEY, D.D.S.

PUBLICATIONS COMMITTEE OF THE MEDICAL STAFF: E. CLARENCE RICE, M.D.; FREDERIC G. BURKE, M.D.; HANS G. KEITEL, M.D.; PRESTON A. MCLENDON, M.D.; MARSHALL PARKS, M.D.; ROBERT H. PARROTT, M.D.; AND JOHN A. WASHINGTON, M.D.

PUBLISHED MONTHLY BY THE STAFF AND RESEARCH FOUNDATION OF THE CHILDREN'S HOSPITAL, WASHINGTON, D. C.

Cases are selected from the weekly conferences held each Sunday morning at 11:00 A.M., from the Clinico-pathological conferences and from the monthly Staff meeting.

This bulletin is printed for the benefit of the present and former members of the Attending and Resident Staffs, and the clinical clerks of Georgetown and George Washington Universities.

Subscription rate is $2.00 per year. Those interested make checks payable to "Clinical Proceedings Dept.," The Children's Hospital, Washington, D. C. Please notify on change of address.

Copyright 1955, Children's Hospital

Entered as second class matter November 21, 1946 at the post office at Washington, D. C., under the Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 538, Act of February 28, 1925, authorized January 17, 1947.

CHILDREN'S HOSPITAL

WASHINGTON 9, D. C.

ANNOUNCEMENT

1954 Clinical Proceedings • ***Attractively Bound Volumes***

Orders are now being taken for bound volumes of the 1954 issues of Clinical Proceedings (268 pages).

The volumes will have a durable and attractive hard cover suitable for display in office or inclusion in a den library. Perhaps you would like to order the 1954 volume for yourself or for a young medical friend or colleague. The cost will be five dollars.

Will you please send your order and check, payable to Clinical Proceedings, Children's Hospital, before September 1, 1955.

PLEASE CLIP AND RETURN THIS FORM TO THE CLINICAL PROCEEDINGS, CHILDREN'S HOSPITAL

Please send one bound volume of the 1954 Clinical Proceedings to:

NAME_____

ADDRESS_____

_____

GIFT OF_____

Check payable to Clinical Proceedings, Children's Hospital, is enclosed

ADENOMATOUS POLYPS OF THE RECTUM AND COLON IN CHILDREN

Alejandro F. Castro, M.D.

SPECIAL REPORT

This study consists of the clinical observations made in thirty consecutive cases of adenomatous polyps of the rectum and colon in children. Familial polyposis and the adenomatous polyps seen in cases with ulcerative colitis are not included. The reported cases have been separated from a total group of over 350 individuals of all age groups with adenomatous polyps for two reasons: (1) The unique pathological structure of the lesions seen in children as compared with the microscopic picture of the "adult" adenomatous polyp[1, 2]; and (2) The obvious separation of these two lesions by nature herself as evidenced by the paucity of adenomas observed in the teen-age group of individuals.

As far as the pathological structure of these two lesions is concerned, the "adult" adenomatous polyp is uncommon before the third decade, and is composed primarily of proliferative glandular elements. There is little connective tissue stroma forming part of the tumor; it is usually benign (fifteen per cent show malignant degeneration); it is lobulated or papillary, and darker than the surrounding mucous membrane. On the other hand, adenomas seen in children are smoother in appearance, and almost one hundred per cent benign (none of our cases showed evidence of malignant degeneration). A large part of the polyp is composed of connective tissue elements with chronic inflammatory reaction and frequently with areas of liquefaction necrosis, granulation tissue, and other evidence of degenerative changes. They are usually the same color as the mucous membrane. In the stroma of these polyps numerous eosinophilic leucocytes are seen. This is responsible for the hypothesis attributing an allergic origin to these structures. Figures 1 and 2 show the differences between the two growths.

The incidence of adenomatous polyps in children with proctological complaints varies between four and eight percent[3, 4]. Excluding anal fissure, adenomatous polyps are the most common cause of bleeding in children. All of the thirty patients whose cases are presented here came to our clinic with painless bleeding as their chief complaint. The blood passed was fresh and the amount usually small. In five of these patients, the tumor protruded through the anal canal and was seen by the child's parents. Of the thirty cases, eleven occurred in girls and nineteen in boys. Most of the polyps (nineteen cases) were located in the rectum in an area

between three and six inches from the anal margin. Therefore, a careful digital-rectal examination will, in most cases, bring to light the source of bleeding in these children. Four children had adenomas located in the sigmoid, four in the descending colon, and one in the transverse colon. Five cases showed multiple adenomas (two to five in number), two in the same localized segment of bowel (so called segmental polyposis), and three in widely separated areas. A barium enema was done in every case. This procedure is strongly recommended in children with adenomas because of the occurrence of multiple lesions in about five to ten percent of

Fig. 1. Childhood type of adenomatous polyp. Notice the large amount of fibrous tissue that enters into the formation of these tumors. × 45

the cases. Adenomatous polyps were seen most frequently in children between the ages of three and five years (Fig. 3). There were two cases seen in children between the ages of twelve and nineteen years. One of the cases in this group was a girl nineteen years of age and is included in this presentation because of the pathological identity with the childhood type of adenoma. One explanation for the paucity of adenomas observed in the second decade of life is the spontaneous passage of these structures. This was well demonstrated by one child nine months old, who passed a rectal adenoma during the course of a barium enema examination. This spontaneous passage may occur in some cases because of the

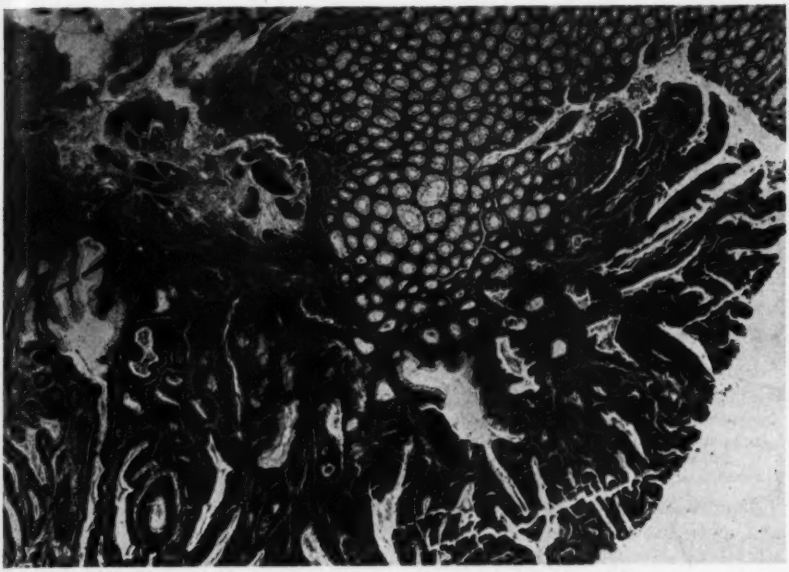


Fig. 2. "Adult type of adenomatous polyp. Notice the large amount of glandular formation as compared to the smaller amount of stoma. × 12½

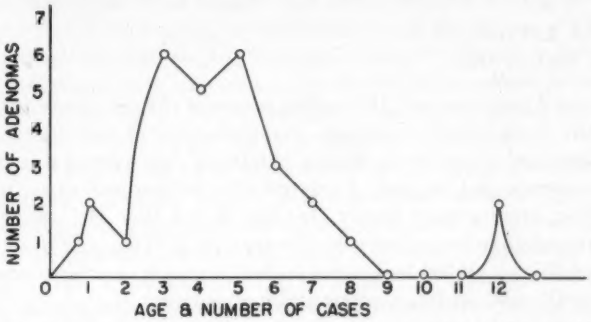


Fig. 3. Table demonstrating the incidence of adenomatus polyps in children of different ages.

amount of degeneration present in the growths as demonstrated microscopically. Such degeneration and passage may account in part for the scarcity of adenomatous polyps in individuals between the ages of twelve and twenty.

The treatment of these polyps varied according to their location and the ease with which the tumor could be intussuscepted through the anal

canal. Five children were seen in consultation only, and treatment was carried out elsewhere. Most of the ones treated at the Proctology Clinic of Washington were removed with the aid of a snare and the base was electrocoagulated. The adenomas present in the transverse, descending, and sigmoid colon were all removed by trans-colonic excision after ligature of the pedicle. There was no morbidity or mortality in these cases.

In conclusion, the microscopic pathological picture of adenomatous polyps in children differs from that seen in the more common adenomas in adults. Even though the chance of malignant degeneration in these adenomatous polyps is extremely small, their removal should be general practice because of continued bleeding and the minimal risk involved in the procedure.

REFERENCES

1. Castro, A. F., et al.: Adenomatous Polyps of the Colon and Rectum. *Surg. Gyn. Obst.* **92**: 164–171, 1951.
2. Helwig, E. B.: Adenomas of the Large Intestine in Children. *Am. J. Dis. Children*, **72**: 289, 1946.
3. Schapiro, S.: the Occurrence of Proctologic Disorders in Infancy and Childhood. A statistical review of 2700 cases, *Gastroenterology*, **15**: 653–666, 1950.
4. Mentzer, C. G.: Pediatric Proctology, *So. Med. Jour.* **41**: 798–803, 1948.

PROPHYLAXIS IN RHEUMATIC FEVER

Special Report

Joseph M. LoPresti, M.D.
John O. Nestor, M.D.

Rheumatic fever is one of the leading causes of chronic illness, invalidism, and death in childhood. Although manifestations of the disease usually make their first appearance during childhood, the effects are projected into adolescence and beyond. A quarter of a million new cases, primarily in children, are reported yearly. During World War II, 100,000 young men were ineligible for military service because of rheumatic heart disease, and an additional 40,000 had either an initial attack or a recurrence of the disease while stationed at various training centers.

At present the mortality rate due to rheumatic heart disease appears to be declining, and it is the impression of many observers that the attack rates of both the initial rheumatic episode and of recurrences also appear to be decreasing. However, the decrease in mortality rates has not been so striking as that of the common infectious diseases, with the exception of poliomyelitis. Whether this apparent decline in the mortality and morbidity of rheumatic fever is due to changes in the natural history of the disease, to the improvement of the economic conditions of urban popula-

tions, or to more effective control of streptococcal upper respiratory infections is not known.

Although the general situation in regard to rheumatic fever appears to be improving, this disease still represents a great public health problem. It seems possible that if the prophylactic procedures for decreasing the incidence of initial attacks and recurrences recommended by the American Heart Association come into general use, the mortality and morbidity caused by rheumatic fever may be still further reduced.

STREPTOCOCCAL RELATIONSHIPS

There is now a reasonable consensus that both the initial attack and subsequent recurrences of rheumatic fever usually follow scarlet fever or other respiratory infections due to group A, beta hemolytic streptococci. These organisms are known to occur in eighty per cent of rheumatic patients. Attacks of rheumatic fever occasionally are reported following streptococcal skin infections. However, unless the presence of streptococci in the pharynx of such patients is excluded by throat cultures, it seems possible that the skin lesions may have been preceded or accompanied by an inapparent streptococcal respiratory infection. The common cold, influenza and the contagious diseases of childhood, with the exception of scarlet fever, do not precipitate rheumatic recurrences. Further evidence indicating that group A, beta hemolytic streptococci bear a specific relationship to rheumatic fever sequels has been obtained by the prophylactic administration of penicillin or sulfonamides. If streptococcal pharyngitis is prevented by this means, rheumatic subjects escape recurrences. At present, however, it is not known whether streptococci act in conjunction with some other agent or are the sole cause of rheumatic fever, and, if so, by what special mechanism they produce the disease.

The development of acute rheumatic fever in rheumatic patients after streptococcal infections follows a characteristic pattern. The attack of streptococcal pharyngitis may be extremely mild or moderately severe and has been designated by Coburn as Phase I. In most instances the symptoms subside quickly and are followed by a "latent" or "silent" period (Phase II) usually lasting one to three weeks, during which the patient is symptom free. Phase II is followed by the onset of acute rheumatic fever, designated as Phase III. After outbreaks of streptococcal pharyngitis or scarlet fever, often caused by an encapsulated strain of a single type, a high percentage of rheumatic children have a recurrence of rheumatic fever. A child who escapes a rheumatic recurrence in one outbreak subsequently may develop rheumatic manifestations after another attack of streptococcal pharyngitis.

Studies of group A hemolytic streptococci associated with the develop-

ment of rheumatic recurrences indicate that the respiratory infection may be caused by any of the forty or more specific types. The regular occurrence of a latent period (Phase II) in addition to the fact that it is impossible to demonstrate streptococci in the affected tissues or in the blood during an acute attack (Phase III) has suggested to several observers that hypersensitivity to these micro-organisms or their products might be the cause of rheumatic fever. The similarity of the symptoms of serum sickness to those of rheumatic fever has lent support to this view.

In recent years knowledge of various enzymes produced by group A hemolytic streptococci has increased. Further studies may show that the characteristic lesions of rheumatic fever are due to enzymatic action on connective tissue either by streptococcal enzymes themselves, or by the catalytic effect of some streptococcal derivative on enzymes already present in the body. A streptococcal proteinase has recently been isolated which produces changes in the myocardium of experimental animals but without the typical Aschoff bodies. The latent period observed after streptococcal pharyngitis might be the time necessary for a sufficient number of connective tissue cells to be injured to produce detectable clinical symptoms.

Though some occasional children who have no preceding history of acute rheumatic fever are found to have rheumatic heart disease, in most instances serious cardiac damage is the result of repeated attacks of active rheumatic fever. The prognosis for children who contract rheumatic fever before they are six years of age usually is graver than for those who have their first attack at a later age. This difference is related principally to the frequency with which carditis is the principal or sole manifestation of the initial attack in the younger age group, and the frequency with which there is residual cardiac damage. Furthermore, young children are more susceptible to streptococcal respiratory infections and thus, are more apt to have frequent recurrences unless adequate prophylaxis is maintained. The outlook for children in whom the rheumatic manifestations are mild with little or no evidence of cardiac involvement is good. Children usually die as a result of further rheumatic infection rather than as a result of mechanical heart failure, and at autopsy fresh as well as old lesions are found. Even with fairly marked valvular deformities the heart is able to function more or less normally, provided the cardiac muscle is in good condition.

RHEUMATIC FEVER PREVENTION

Since severe cardiac damage is usually the result of repeated rheumatic recurrences, the chief concern is to prevent them. Rheumatic patients in the inactive stage of the disease who escape streptococcal respiratory disease also escape rheumatic relapses. Tonsillectomy as a prophylactic

measure is of no value. Susceptibility to attacks of streptococcal pharyngitis is not reduced by removal of the tonsils. The indications for tonsillectomy are the same for rheumatic as for normal children: obviously infected tonsils; a history of frequent sore throats; cervical adenitis; and chronic otitis media. The operation must be performed at a time when the rheumatic process is inactive and the patient is free of respiratory infection. Rheumatic children are prone to develop subacute bacterial endocarditis, and a transient bacteremia frequently follows operative procedures such as tonsillectomy or dental extractions. Rheumatic patients should, therefore, receive prophylactic penicillin immediately before such elective surgical procedures. Adequate prophylaxis will be afforded by a single injection of 600,000 units of benzathine penicillin G administered three days before operation.

Rheumatic fever is a recurrent disease which in most instances can be prevented. Since both the initial and recurrent attacks of the disease are precipitated by infections with beta hemolytic streptococci, prevention of rheumatic fever and rheumatic heart disease depends upon the control of streptococcal infections. This may be accomplished by: (1) prevention of streptococcal infections in rheumatic subjects; and (2) early and adequate treatment of streptococcal infections in all individuals.

In many instances streptococcal infections can be recognized by their clinical manifestations. In some patients, however, it is difficult or impossible to determine the streptococcal nature of a respiratory infection without obtaining throat cultures. The common symptoms include sore throat, sudden in onset and accompanied by dysphagia. Headache is a common complaint. Fever is variable but generally ranges from 101 to 104 degrees. In children, abdominal pain will be a frequent symptom, and nausea and vomiting often will occur. The common physical findings include a red throat, an exudate, and tender cervical lymph nodes. The white blood count generally will be over 12,000 and a positive throat culture for beta hemolytic streptococci is almost always diagnostic. In the absence of the common symptoms and signs, coryza, hoarseness, and cough usually are not associated with a streptococcal infection.

When streptococcal infection is suspected, treatment should be started immediately. Penicillin is the drug of choice. Effective blood levels should be maintained for a period of ten days to prevent rheumatic fever by eradicating the streptococci from the throat. Penicillin may be administered by either intramuscular or oral routes. Intramuscular administration is recommended as the method of choice since it insures adequate treatment. Oral therapy by contrast is dependent on the cooperation of the patient. On the other hand, some physicians and patients prefer repeated oral medication and object to injections. In children one

intramuscular injection of 600,000 units of benzathine penicillin G or an injection of 300,000 units of procaine penicillin with aluminum monostearate in oil every third day for three doses will provide adequate therapy. For oral medication 250,000 units of benzathine penicillin G tablets three times a day for a full ten days is the recommended treatment. To prevent rheumatic fever by eradicating streptococci, *therapy must be continued for the entire ten days even though the temperature returns to normal and the patient is asymptomatic.* The broad spectrum antibiotics are less effective than penicillin and should be used only if the patient is allergic to penicillin. Terramycin, aureomycin and erythromycin have been shown to be effective in decreasing the incidence of rheumatic fever. When using these drugs, full therapeutic dosage should be given for a period of ten days. Since the sulfonamides are only bacteriostatic, there is some evidence which suggests that they may not prevent rheumatic fever when used to treat acute streptococcal infections and therefore antibiotics are preferable for this purpose.

PREVENTION OF RECURRENCES

Many streptococcal infections occur without producing clinical manifestations. For this reason, prevention of recurrent rheumatic fever must depend on continuous prophylaxis rather than solely on treatment of acute attacks of streptococcal disease. All individuals who have a well established history of rheumatic fever or chorea or who show definite evidence of rheumatic heart disease should be placed on continuous prophylaxis. As soon as the diagnosis of rheumatic fever is made or any time thereafter when the patient is first seen treatment should be instituted. The streptococcus should be eradicated with penicillin following which the prophylactic regimen is instituted. In inactive rheumatic fever, treatment should be started when the patient is first seen. Prophylaxis should be continued throughout life or until new knowledge makes this recommendation invalid. A more practical suggestion for the length of prophylactic treatment is the recommendations of the Heart Association of Maryland. In adults, prophylaxis should be carried out for a period of at least five years from the last attack. In children prophylaxis should be continued at least until the age of eighteen. Treatment should continue throughout the year including the summer months since streptococcal infections can occur at any season, although they are more prevalent in the winter. Patients who are being followed as rheumatic suspects should be on prophylactic treatment until a conclusion has been reached that they do not have rheumatic fever, at which time treatment may be discontinued.

Sufficient information has been accumulated to indicate that long

acting oral and intramuscular penicillin are effective prophylactic agents. Penicillin has the advantage of rarely producing serious toxic reactions, particularly when it is administered by the oral route. It is desirable also for its bacteriocidal effect on hemolytic streptococci, as well as the fact that no penicillin–resistant strains have been reported. Penicillin has the disadvantage of being more costly than sulfonamides but the overall cost may not be greater since laboratory follow-up is unnecessary. For the majority of individuals the oral method of administration is preferable. The intramuscular injection of long-acting penicillin is advisable in those patients who have proved uncooperative in taking daily medication. In most instances failures of prophylaxis occur in patients who fail to ingest the drug regularly. For oral prophylaxis 250,000 units of the benzathine penicillin G tablets or straight penicillin G tablets twice a day, should be prescribed. By injection, 1,200,000 units of benzathine penicillin G once a month will be adequate. Toxic reactions tend to be more frequent and more severe with the parenteral penicillin and include urticaria, serum-sickness-like reactions, and angioneurotic edema. Although many individuals who have had reactions to penicillin subsequently may be able to tolerate the drug, it is safer not to use penicillin if the reaction has been severe and particularly if angioneurotic edema has occurred. When reactions to penicillin occur or if there is a history of previous reactions to this antibiotic, prophylactic treatment should be continued with a sulfonamide.

The advantage of the sulfonamides (sulfadiazine, sulfisoxazole) is that they are inexpensive. The main disadvantage is the possibility of toxic reactions such as agranulocytosis. Although such reactions are not common, it is still necessary to follow the blood count. This adds to the total cost of the prophylactic program. In addition, the fear of toxic reactions has made many physicians reluctant to use a sulfonamide over a long period of time. This has diminished its effectiveness as a prophylactic agent for general use. For these reasons oral penicillin is recommended as the drug of choice. Sulfadiazine and sulfisoxazole represent valuable alternative agents for those who cannot tolerate penicillin. The dose for children under 60 pounds is 0.25 grams twice a day; and for those over 60 pounds, 0.5 grams twice a day. Toxic reactions include skin eruptions, leukopenia, and hematuria. White blood counts are advisable every two weeks for the first six weeks and at least every three months thereafter. Toxic reactions are rare after eight weeks of sulfonamide therapy. If a toxic manifestation should occur, the drug should be discontinued. In the rare patient who is sensitive to both penicillin and the sulfonamides, aureomycin may be used. The other broad spectrum antibiotics may be effective, but no extensive clinical trials have been reported.

BIBLIOGRAPHY

BALDWIN, J. S.: Sulfadiazine prophylaxis in children and adolescents with inactive rheumatic fever, *J. Pediat.* **30**: 284–288 (March) 1947.

BREESE, B. B., AND OTHERS: *Mod. Concepts Cardiovas. Dis.*, **22**: 158, 1953.

BREESE, B. B.: *J.A.M.A.*, **152**: 10, 1953.

CHAMOVITZ, R., AND OTHERS: Prevention of rheumatic fever by treatment of previous streptococcal infections. I. Evaluation of benzathine penicillin G, *New England J. Med.*, **251**: 466–471 (Sept. 16) 1954.

COBURN, A. F., AND MOORE, L. V.: The prophylactic use of sulfanilamide in streptococcal respiratory infections, with especial reference to rheumatic fever, *J. Clin. Investigation*, **18**: 147–155 (Jan.) 1939.

DENNY, F. W., WANNAMAKER, L. W., BRINK, W. R., RAMMELKAMP, C. H., AND CUSTER, E. A.: *J.A.M.A.*, **143**: 151, 1950.

HOUSER, H. B., AND ECKHARDT, G. C.: Recent developments in the prevention of rheumatic fever, *Ann. Int. Med.*, **37**: 103501043 (Nov.) 1952.

JONES, T. D. AND BLAND, E. F.: *Tr. A. Am. Physicians*, **57**: 265, 1942.

KUTTNER, A. G., AND REYERSBACK, G.: *J. Clin. Investigation*, **22**: 77, 1943.

MARKOWITZ, M. AND KUTTNER, A. G.: *J. Pediat.*, **31**: 1, 1947.

MASSELL, B. F., AND OTHERS: Prevention of rheumatic fever by prompt penicillin therapy of hemolytic streptococcic respiratory infections: progress report, *J.A.M.A.*, **146**: 1469–1474 (Aug. 18) 1951.

RANTZ, L. A.: The Prevention of Rheumatic Fever, Charles C Thomas, 1952.

STOLLERMAN, G. H., AND RUSOFF, J. H.: *J.A.M.A.*, **150**: 1571, 1952.

THOMAS, C. B., FRANCE, R., AND REICHSMAN, F.: Prophylactic use of sulfanilamide in patients susceptible to rheumatic fever, *J.A.M.A.*, **116**: 551–560 (Feb. 15) 1941.

WANNAMAKER, L. W., AND OTHERS: The effect of penicillin prophylaxis on streptococcal disease rates and the carrier state, *New England J. Med.*, **249**: 1–7 (July) 1953.

WRIGHT, S., PURCELL, E. M., KASS, E. H., AND FINLAND, M.: *J. Lab. & Clin. Med.*, **42**: 417, 1953.

ACUTE NEPHRITIS COMPLICATING AN ILLNESS RESEMBLING INFECTIOUS MONONUCLEOSIS

A Case Report

George J. Cohen, M.D.

Infectious mononucleosis is a disease of protean manifestations, both clinically and on laboratory study. The diagnosis is an easy one when the classical findings are present. These include sore throat, fever, lymph node enlargement, splenomegaly, lymphocytosis with atypical lymphocytes, and an elevated heterophile antibody titer. However, when all the typical findings are not present the diagnosis is considerably more tenuous; and, since no specific etiology has yet been determined, an atypical case provokes much speculation. Because the following case was not classical in all its manifestations and because it presented the unusual complication of hemorrhagic nephritis, it was felt worth presenting for consideration as a problem in diagnosis.

CASE REPORT

This eleven year old white male was admitted to the hospital on December 3, 1954 with a five-day history of pain in both sides of his neck on motion, anorexia, lassitude and fatigability. Four days before admission

there developed a low grade fever which was controlled with aspirin, and three days before admission the boy's neck became swollen. Two days before admission he was seen in the Out Patient Department where examination was normal except for temperature of 100°, a right anterior cervical lymph node 3.5 cm. in diameter and small (less than one cm.) nodes in the left cervical chain and both axillae. Tuberculin (P.P.D. intermediate strength) and histoplasmin skin tests were negative.

On admission this was a well developed and nourished, slender boy who was not acutely ill. The significant physical findings were temperature of 101°, a thin mucoid nasal discharge, injection and lymphoid hyperplasia of the pharynx. The tonsils had been removed. The heart was normal except for a short blowing systolic murmur, best heard in the third and fourth left intercostal space at the sternal border. The liver and spleen were both fairly firm and each was felt about 3 to 4 cm. below the costal margins. Lymph node survey showed a tender, firm node, 3 cm. in diameter, under the belly of each sternomastoid muscle with shotty non-tender nodes in the anterior and posterior cervical chains, epitrochlear areas, axillae, and groins. The remainder of the physical examination was normal except for a blood pressure of 140/90.

On admission, urinalysis showed 150 mg. per cent of albumin, many red blood cells, 15–25 white blood cells per high power field, a few casts, and few epithelial cells. The white blood cell count was 8,500 with 60 per cent segmented neutrophiles, 14 per cent bands, 19 per cent lymphocytes, 5 per cent monocytes and 2 per cent eosinophiles. Typhoid, paratyphoid and heterophile agglutinations were negative on admission. Chest x-ray and electrocardiograms were normal. A blood culture was sterile. A throat culture was not taken.

In the hospital the patient had a fever between 99° and 100.6° until December 8th after which he remained afebrile. On December 4th the patient complained of right earache and examination revealed minimal injection of the periphery of the drum. On December 5th the right drum showed several clear and hemorrhagic vesicles, and the left drum was somewhat dull with injection of the periphery. Penicillin and sulfonamides were administered but on December 6th the left drum perforated, draining a mucopurulent material which showed no growth on culture.

His urine showed a gradual decrease in albumin, and by December 8th was albumin free. By December 10th the urine showed no more casts and by December 13th there was no more hematuria. However, on December 22nd the urine contained many bacteria and occasional leucocytes and a culture showed growth of alpha hemolytic streptococci. There was never any clinical evidence of edema and his eye grounds appeared normal during the entire hospital stay. The blood pressure gradually declined

from an initial reading of 140/90 to a level of 104/70 by December 14th.

On December 7th, the sedimentation rate was 33 mm/hr. (Wintrobe), BUN was 20 mg. per cent and total protein was 6.9 grams per cent with A/G ratio of 1.5/1. On December 10th the typhoid and paratyphoid agglutinations were still negative; the heterophile titer had risen to 1:56; anti-streptolysin O titer was 125 units (normal); and C-reactive protein was 1 plus. On December 13th the leucocyte count on peripheral blood was 7,600 with 36 per cent lymphocytes, four of which were atypical. Throughout the course of illness the total white cell count was consistently below 8,500. On December 7th there were 43 per cent lymphocytes, 4 per cent monocytes and 8 per cent eosinophiles; on December 20th there were 44 per cent lymphocytes, 7 per cent monocytes and 7 per cent eosinophiles. The sedimentation rate on December 13th was 27 mm/hr., and the heterophile antibody titer had risen to 1:112. By December 20th the BUN had dropped to 16.5 mg. per cent; the heterophile titer was still 1:112; the C-reactive protein had become negative; the sedimentation rate dropped to 21 mm/hr.; and the ASO titer remained 125 units. After absorption with guinea pig kidney, the titer of heterophile antibody was 0. This absorption procedure was performed only on one occasion.

Clinically the patient was asymptomatic by December 10th when his ear ceased draining, his liver and spleen were no longer palpable, and his adenopathy had subsided markedly. By December 15th his ear drums appeared somewhat dull and retracted, but showed no evidence of inflammation. The sulfonamides and parenteral penicillin were stopped and oral penicillin prescribed. At this time the cardiac murmur was no longer heard.

Although there were no urinary symptoms, sulfisoxizole was given for one week in an attempt to clear the urine of the infection which was noted by culture. After discharge on December 23rd, the youngster remained asymptomatic and was re-evaluated in the Out Patient Department on January 1, 1955, at which time he was entirely well and the physical examination was quite normal. Urinalysis was normal; sedimentation rate was 6 mm/hr.; C-reactive protein was negative; and presumptive heterophile was positive at 1:56. The white blood cell count was 7,800 with 47 per cent lymphocytes, 1 per cent of which were atypical, 6 per cent monocytes, 6 per cent eosinophiles, 1 per cent basophile, 34 per cent segmented neutrophiles and 6 per cent band forms.

DISCUSSION

The problem of nephritis in infectious mononucleosis is not a common one, and many standard texts make no mention of it. Sprunt states that six per cent of patients with infectious mononucleosis have a nephritis which is mainly a hematuria without other findings.[1] Rivers and Gorham

each comment that nephritis is a rare complication.[2, 3] In an analysis of 556 cases of infectious mononucleosis, Sleeth found that three per cent showed albuminuria and most of these also had cells in the urine.[4] In describing the pathology, Krugman noted a perivascular infiltration of normal and atypical lymphocytes in the kidney.[5] Although our patient had many of the classic features of nephritis, including albumin, casts, and cells in the urine, and an elevated blood pressure and BUN, his course was much shorter and milder than we see in most of our cases of nephritis. Unfortunately, no throat culture was taken, but there was no evidence of streptococcal infection on blood and ear culture, and the anti streptolysin titer remained normal throughout. Therefore, it is quite unlikely that this was a typical post-streptococcal nephritis. We felt that the urinary infection was a coincidental problem especially in view of the late onset after the nephritic findings had disappeared.

It is interesting to note that this boy's sedimentation rate was elevated during his symptomatic period. Although most writers state that the sedimentation rate is usually normal, and many make no mention of it, LoPresti, et al., tested five patients at random in a group of thirty-four with infectious mononucleosis, and all five patients had rapid sedimentation rates.[6] This would seem to attest to the non-specific nature of the test.

The classical laboratory findings of elevated heterophile antibody titer and the presence of atypical lymphocytes are known for their evanescence. The characteristic lymphocytes may frequently be found only by daily examination of a peripheral blood smear. Certainly in our patient such cells were observed only twice; however, the persistent relatively high eosinophile and monocyte counts are frequently seen in infectious mononucleosis.

As for the heterophile test, it is interesting that Davidsohn states, and most other authors agree, that the presence of an elevated titer after guinea pig kidney absorption is specific for infectious mononucleosis;[7] yet Rivers, Krugman and other authors state that the heterophile titer may be positive in as few as fifty per cent of the cases.[2, 5] LoPresti, et al., tested thirty-one otherwise classical cases in a series of thirty-four and found negative heterophile antibody titers in twenty-one.[6] Davidsohn feels that high non-specific titers in the presence of other evidence consistent with infectious mononucleosis point to the diagnosis of "lymphocytic angina" which should be considered a distinct disease of separate etiology.[7]

It would seem obvious that, until a specific etiology is determined for infectious mononucleosis, diagnosis will remain a problem in all but the most classical case. Whether the atypical cases will be proved to have

other causes is a matter for speculation and study. Meanwhile, in the absence of other diagnostic probabilities and in the presence of strongly suggestive features for infectious mononucleosis, such a diagnosis is probably justified, and argument would be more academic than practical.

In summary, this is a case with many features consistent with a diagnosis of infectious mononucleosis, complicated by a nephritis which seems to have been part of the primary disease. The lack of a specific etiology and the difficulties in accurate diagnosis are discussed.

REFERENCES

1. Sprunt, Thomas P.: Brennemann's *Practice of Pediatrics*, Vol. II, Chapter 8, W. F. Prior Co., Hagerstown, Md., 1951.
2. Rivers, Thomas M.: *Viral and Rickettsial Diseases of Man*, 2nd Ed., J. B. Lippincott Co., Philadelphia, 1952.
3. Gorham, L. W.: Cecil's *Textbook of Medicine*, 7th Ed., P. 515, W. B. Saunders Co., Philadelphia, 1947.
4. Sleeth, Clark K.: Infectious Mononucleosis, *West Virginia Medicine*, **48**: 143, 1952.
5. Krugman, Saul: Holt *Pediatrics*, Holt & McIntosh, 12th Ed., Appleton-Century-Crofts, New York, 1953.
6. LoPresti, J. M., Kaufman, P., and Rice, E. C.: Infectious Mononucleosis In Childhood *Clinical Proceedings, Children's Hospital*, **6**: 1949.
7. Davidsohn, I.: Serologic Diagnosis of Infectious Mononucleosis, *J.A.M.A.*, **108**: 289, 1937.

CLINICOPATHOLOGICAL CONFERENCE

Discussant: Dr. George W. Ware

PROTOCOL

This nine month old white girl was admitted to the Hospital on February 20th and died on February 22nd at 8:10 a.m. The patient was said to have been in excellent health until four days prior to admission when she began to gag and she vomited several times. Following this, slight respiratory distress occurred. On the day prior to admission, fever and moderate dyspnea developed, at which time penicillin and "white medicine" were prescribed by her local physician.

On the morning of admission the temperature was 106°. There was severe dyspnea with an excess of frothy sputum. No other symptoms were recalled. There had been no known toxic ingestants.

The birth and neonatal period were uneventful; the child weighed nine pounds at birth and did well on an evaporated milk formula with supplement of baby foods and vitamins. The father and one sibling were reported to be in good health.

The appearance of the patient on admission was striking in that she was pallid and in marked respiratory distress, with a temperature of 106°. The infant was well developed and well nourished. The fontanel was not

bulging. An excess of white viscid mucus was noted in the mouth and throat. The heart rate was 160 per minute. Rhonchi and fine rales were observed throughout both lung fields with intercostal retraction of the chest and respiratory rate of 100. The liver edge was palpable 4 cm. below the costal margin. Because the child was so severely ill, no chest x-ray was taken.

Admission laboratory examination showed a red blood count of 3.5 million per cubic millimeter with 8 grams of hemoglobin per 100 cc. of blood. The total leukocyte count was 11,800 with a slight predominance of granulocytes. *Bacillus subtilis* was cultured from the blood. The throat culture showed only normal throat flora.

Following admission the patient was immediately placed in an oxygen tent and cold packs, ice enemas, and alcohol sponges were administered to lower the temperature. Digitoxin and massive doses of penicillin and chloromycetin were given. The respirations improved somewhat within twenty-four hours. There was some clearing of the rales in the lungs, but throughout the night moderate cyanosis developed and the patient expired.

DISCUSSION

We are presented today with the clinical picture of a nine month old infant who, with few symptoms, developed an acute fulminating illness and died within six days.

The primary symptom was related to the gastro-intestinal tract: vomiting. Thereafter, there is nothing to give attention to this system. The two systems which could possibly play the fatal role appear to be respiratory and/or cardiac.

The conditions which might cause this catastrophic illness include:

1. Aspiration pneumonitis
2. Acute laryngotracheobronchitis
3. Meningococcic septicemia
4. Miliary tuberculosis
5. Acute congestive heart failure secondary to coarctation of aorta
6. Aspiration of a foreign body.

1) *Aspiration pneumonitis:* Here we speak of aspiration of formula. This may occur during the actual feeding or be secondary to regurgitation. Such aspiration causes damage by mechanical blockage of a segment of the lung as a result of diffuse chemical pneumonitis. Such an occurrence could explain the vomiting, severe respiratory difficulty, and fever. However, aspiration pneumonitis usually occurs subsequent to two conditions: a) Blockage of the gastro-intestinal tract by some anatomic lesion such as pyloric stenosis and intestinal atresia. This causes repeated vomiting with exhaustion of defense mechanisms; b) Debilitation, the result of some systemic disease destroying the normal defenses of the infant. Neither

of these conditions seems to be met since the infant is described as "in excellent health prior to illness".

2) *Acute laryngotracheobronchitis:* This entity in its fulminating form is indeed a dreadful disease and one which makes me distinctly uneasy. It is rapidly progressive, frequently caused by *H. influenzae*, and attended by severe dyspnea and cyanosis, high fever, and especially *toxicity*. Dyspnea is mainly inspiratory due to laryngeal involvement. Examination of lung fields usually reveals mild to moderate bilateral rales. The patient usually has an exhausting, ineffective cough.

There are some features which fit this case but not perfectly. Inspiratory difficulty was not a marked feature. Tracheotomy was apparently not considered and not performed. Since one of the prime features of this condition is struggling to get air into the alveoli, I believe we can dismiss this.

3) *Meningococcic septicemia:* Such a systemic infection may start out with mild respiratory symptoms and then rapidly progress to death. The disease is usually attended by fever, vomiting, and toxicity. To my mind, skin lesions are prominent features of this illness and these develop rapidly and early in the course of the illness. No rash is noted.

4) *Miliary tuberculosis:* This entity, when it occurs, is a complication of the primary form of tuberculosis. There is a sudden onset, high fever, and toxicity. Examination of the lungs may reveal only diffuse rales, and the x-ray may be negative. This patient's history mentions no contact with tuberculosis and a tuberculin test was not done. Miliary tuberculosis as a rule does not kill this rapidly; the disease runs its course in several weeks to several months.

5) *Cardiac conditions* such as *acute heart failure* secondary to *coarctation of aorta:* There are certain features which point to a cardiac etiology such as onset with slight respiratory distress; excess mucus; heart rate of 160; palpable liver and rales in both lung fields. Considering cardiac lesions in an infant whose neonatal period is described as "uneventful" and who presumably was under pediatric care, one is struck with the possibility of a coarctation of the aorta. Such a condition can cause sudden progressive heart failure.

In 1903 Bonnet classified coarctations into two groups: a) *Infantile:* In this condition the coarctation exists *above* the insertion of the ductus arteriosus into the aorta; b) *Adult:* The coarctation exists at or below the insertion of the ductus into the aorta. In the infantile variety with a patent ductus there is no stimulus to the formation of a collateral circulation. The right ventricle pumps blood through the ductus arteriosus into the distal aorta. When the ductus closes, there is an immediate stress placed on the left ventricle which often goes into failure. Survival depends on the development in this critical period of a collateral circulation. How-

ever, it is difficult for me to assume that the disease is cardiac in origin. The evidence seems to point too strongly to a respiratory entity. So we seem to be left with the final diagnosis.

6) *Aspiration of a Foreign Body:* In this regard, to my mind, the most important point of the history is the following: "In excellent health until four days prior to admission when she began to gag and vomited several times." Following this, "a slight respiratory distress occurred". Then following an asymptomatic period, severe symptoms appeared. Such a history is most significant and, regardless of the remainder of the protocol, a foreign body in the respiratory passages must be ruled out.

Often the diagnosis of a foreign body is not considered in such cases. This is due to two factors: no one actually sees the foreign body in the infant's mouth; and there is an asymptomatic period. Perhaps in this case, because of the mother's illness the patient was not so well watched as usual. In any event, no chest film was taken because the child was critically ill when admitted to the hospital.

After the asymptomatic period, the difficulties progressed. There was severe dyspnea and "an excess of frothy sputum" because of respiratory obstruction. Infection due to obstruction occurred, causing fever and toxicity. There were rales in both lung fields because the object was most likely tracheal in location or probably was organic in nature.

The respiratory rate rose to 100; respiratory difficulty progressed; and "intercostal retraction of the chest" was noted. The patient temporarily improved, with supportive measures. However, the basic cause, a respiratory foreign body, was not removed and the infant succumbed.

My diagnosis is a foreign body of the respiratory passages either organic in nature or of sufficient size to block the trachea.

A few statements concerning foreign bodies of the air or food passages are pertinent. The age of the patient is of no importance as the aspiration of foreign bodies has been reported in infants one day old. Such accidents may occur as a result of carelessness on the part of the person taking care of the child or may follow the giving of an unfamiliar food. The history is practically always given to the physician by the parents or the incriminating symptoms can be elicited by direct questioning.

The symptoms are choking or vomiting followed by an asymptomatic period. Shortly after this, cough, dyspnea and wheezing, usually unilateral, occur. The physical examination may be entirely negative. Inspiratory and expiratory phase x-rays of the chest should be taken. The physical signs when present are obstructive emphysema with hyperresonance on percussion. This is brought about because the air gets past the object on inspiration, but not on expiration. The lung becomes larger on the affected side and displaces the diaphragm downward on this side. The mediastinum shifts to the unaffected side. Atelectasis, the other physical sign, follows when the

object completely blocks the bronchus. The mediastinum is retracted to the affected side and the homolateral diaphragm is elevated. Treatment consists of bronchoscopic examination on *the history alone* even if physical examination and x-rays are negative.

PATHOLOGY

The significant findings at autopsy were confined to the chest. An open safety pin was found in the esophagus, perforating the posterior wall 3.0 cm. inferior to the level of the larynx. An abscess 3.0 cm. in diameter surrounded the pin and the external surface of the abscess was bounded anteriorly by the external surface of the trachea and esophagus, laterally by the parietal pleura of the right lung, and posteriorly by the fascia overlying the vertebral column. A focal acute pneumonitis was noted microscopically in the adjacent lung tissue and the tracheal and esophageal walls revealed marked acute inflammatory change.

Dr. Ware's diagnosis: Aspiration of foreign body
Clinical diagnosis: Pneumonitis
Pathological diagnosis: Ingestion of safety pin in esophagus with perforation.

EDITORIALS

SUGGESTED METHOD OF SCORING FOR A TISSUE COMMITTEE

The Tissue Committee of Children's Hospital, as provided for in the By-Laws of the Medical Staff, was appointed on March 18, 1954. It is comprised of two surgeons and a pathologist.

The first meeting of the Committee was held in April 1954, at which time the Pathology Report for the months of January, February, and March was reviewed. After considerable discussion it was decided the Committee should confine its activities to reviewing and evaluating only cases of appendectomy.

After a brief period of trial and error the present system of scoring was evolved and as of June 1954 a careful review of all cases of appendectomy has been carried out and each case graded by the Committee.

Under the present system of scoring all surgeons performing appendectomies are assigned a code number which is placed on a small index card. The hospital number of every appendectomy performed by a particular surgeon is recorded on his card and opposite this a grade is assigned after careful review of the chart by the Committee.

The method of scoring follows:

Charts Reveal	Score
Justified operation—diagnosis correct	1.
Justified operation—diagnosis incorrect	2.
Questionable justification	3.
Unjustified operation—diagnosis incorrect	4.
Unnecessary delay in operating	.1
No substantiating notes by surgeon	.01
No notes or inadequate notes by House Staff	.001

(Example—Perfect Score.... 1.000)

This system of grading has been kept simple so that a glance at any particular surgeon's card will show clearly the number of justified operations, unjustified operations, or other scoring points. Thus the surgeons with the highest number of correct diagnoses and well substantiated records will have the lowest grade.

Between June 1, 1954, and January 31, 1955, there were one hundred and twenty-one appendectomies performed at Children's Hospital by forty-one different surgeons and the resident surgeons.

With this comparatively small number of cases operated upon by so many different surgeons no definite conclusions can be drawn at this time; however, several suggestions may be made.

A number of the cases receiving a grade of 3 (questionable justification) or grade of 4 (unjustified operation) would have received a better grade if the attending surgeon had taken time more often to document his case by making an adequate preoperative note. The Tissue Committee should serve as a stimulus for improving the charts with careful and adequate preoperative notes.

This method of recording the findings of the Tissue Committee is believed to be original with Children's Hospital. Though simple, it has been found most satisfactory and has kept the work and records of the Committee to a minimum. It makes data on the cases easily available and furnishes information as to the caliber of work done.

Ralph D. Whitley, M. D.

UNSURPASSED

HYPOALLERGENIC

SOYA FORMULA

MILK-FREE

FOR INFANTS

. . . due to exclusive formulation and dramatic new processing methods

Physical advantages

- pleasant, bland flavor . . . no "burned or raw bean" taste . . . color is light, appetizing, "formula-like."
- exceptionally well tolerated . . . stools satisfactory . . . does not cause diarrhea or other gastrointestinal disturbances . . . babies take feedings well.
- easy to prepare—1 part Liquid Sobee to 1 part water for a formula supplying 20 calories per fluid ounce.

Nutritional advantages

- Liquid Sobee® is a well balanced formula, not a mere "soybean milk" . . . caloric distribution based on authoritative recommendations for infant formulas . . . no added carbohydrate needed.
- new processing methods prevent usual destruction of amino acids and important B vitamins . . . Liquid Sobee supplies 4.8 mg. of iron per quart of normal dilution.

The important first step in management of infant food sensitivities is Liquid Sobee. Because milk is the most common offender,[1,2,3,4] many physicians start infants on Liquid Sobee at the slightest suspicion of food allergy.

Available in 15½ fl. oz. cans

(1) Butler, A. M., and Wolman, I. J.: Quart. Rev. Pediat. 9: 63, 1954. (2) Moore, I. H.: Journal-Lancet 74: 80, 1954. (3) Collins-Williams, C.: J. Pediat. 45: 337, 1954. (4) Clein, N. W.: Ann. Allergy 9: 195, 1951.

LIQUID SOBEE

MEAD JOHNSON & COMPANY • EVANSVILLE, INDIANA, U.S.A. MEAD

MEAD, JOHNSON & COMPANY, Suite 419 Eig Building, 8641 Colesville Road, Silver Spring, Maryland. JUniper 9-1222

D

C

A

S

ssing

taste

does
ances

for a

"soy-
tative
l car-

amino
pplies

nsitiv-
mmon
Sobee

1954.
s, C.:
1951.

E

EAD